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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/216,604	12/17/98	GUO	Y

022249
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EXAMINER	
DIBRINO, M	
ART UNIT	PAPER NUMBER
1644	12

DATE MAILED: 07/20/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/216,604	Applicant(s) Guo, Y.
	Examiner Marianne DiBrino	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 14, 2001*

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *23-84* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *23-84* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 5/14/01 (Paper No. 11), is acknowledged and has been entered.

2. Claims 23-84 are pending and are presently being examined.

The following are new grounds of rejection necessitated by Applicant's amendment filed 5/14/01.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Applicant is reminded of the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999; the following rejection is set forth herein.

Claims 23-84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed method of making, and the composition comprising, antibodies with one or more antigen binding sites for one or more gp55, gp95, gp115 or gp120 antigens on the surface of one or more target hepatocellular carcinoma, lymphoma or colon or gastric cancer cells.

The instant claims encompass antibodies which have antigen binding sites for any glycoprotein antigen on the surface of the said target cells which is of the size 55, 95, 115 or 120 kDa, i.e., "gp55", "gp95", "gp115" or "gp120" and the claims encompass the said glycoprotein antigen of the said size. There is insufficient disclosure in the specification on such said antibodies and glycoprotein antigens.

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of an antigen "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description ... requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; Id. at 1170, 25 USPQ2d at 1606.

The specification further discloses that three monoclonal antibodies were produced which reacted with hepa 1-6 cells and recognized either a 55 kDa, 95 kDa or 210 kDa glycoprotein expressed on most tumor cells as determined by immunoprecipitation. The specification discloses that the said monoclonal antibodies were designated as anti-gp55, anti-gp95 and anti-gp210, respectively (page 24 at lines 19-27). The specification also discloses that bispecific monoclonal antibodies were produced from these antibodies (page 25 at lines 5-18). The specification discloses bispecific antibodies CD28:gp55, CD28:gp95 CD28:gp115 and CD28:gp210 (ibid, see also figures and examples). The specification further discloses CD28:gp55, CD28:gp95, and CD28:gp210 armed HEPA 1-6 (hepatoma tumor cells), CD28:gp55 armed EL-4 (lymphoma cells) and CD28:gp55 armed SMCC-1 (colon carcinoma cells) (examples). The specification also discloses EL-4 or SMCC tumor cell armed -Bi-Mab anti-gp115:anti-4-1BB (4-1BB is a glycoprotein expressed on primed T CD4+ and CD8+ T cells) (Example 8). The specification also discloses primary and E1B deleted Adenovirus-infected liver cells armed with anti-gp115:anti-CD28 (Example 9). The specification discloses rat NTBII tumor cells or fused tumor cells (rat NTBII and mouse SMCC-1) armed with gp115:CD28 Bi-Mab (Example 11).

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as "gp55", "gp95", "gp115", "gp210", without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of being a glycoprotein of 55, 95, 115 or 210 kDa size. It does not specifically define any of the glycoproteins that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than size. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. Many such species may be 55, 95, 115 or 210 kDa in size. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Since the disclosure fails to provide sufficient relevant identifying characteristics that identify members of the genus, and given the broad genus claimed, the disclosure of an antibody to a protein of 55, 95, 115 or 210 kDa on the surface of one type of hepatocellular carcinoma cell line and the proteins of the said sizes is insufficient to describe the genus as broadly claimed. One of skill in the art would not have recognized that Applicant was in possession of the invention claimed in the instant claims.

5. Claims 23-84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to make and/or use the instant invention. The claimed composition, and method of making thereof, comprising one or more isolated or enriched dendritic cells or macrophages which presents one or more gp55, gp95, gp115 or gp210 antigens of hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells and one or more antibodies comprising one or more binding sites for one or more gp55, gp95, gp115 or gp210

antigens encompasses: (1) making and using antibodies to any 55, 95, 115 or 210 kDa glycoprotein, i.e., "gp55", "gp95", "gp115" or "gp210" on the surface of any hepatocellular carcinoma cell, lymphoma cell, colon carcinoma cell or gastric cancer cell. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass a composition which comprises an antibody with a specificity against any cell surface protein on any cancer cell recited in the instant claims. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed compositions can be made and/or used.

The specification further discloses that three monoclonal antibodies were produced which reacted with hepa 1-6 cells and recognized either a 55 kDa, 95 kDa or 210 kDa glycoprotein expressed on most tumor cells as determined by immunoprecipitation. The specification discloses that the said monoclonal antibodies were designated as anti-gp55, anti-gp95 and anti-gp210, respectively (page 24 at lines 19-27). The specification also discloses that bispecific monoclonal antibodies were produced from these antibodies (page 25 at lines 5-18). The specification discloses bispecific antibodies CD28:gp55, CD28:gp95 CD28:gp115 and CD28:gp210 (ibid, see also figures and examples).

The specification discloses working examples of compositions comprising CD28:gp55, CD28:gp95, and CD28:gp210 armed HEPA 1-6 (hepatoma tumor cells), CD28:gp55 armed EL-4 (lymphoma cells) and CD28:gp55 armed SMCC-1 (colon carcinoma cells) (examples). The specification also discloses EL-4 or SMCC tumor cell armed -Bi-Mab anti-gp115:anti-4-1BB (4-1BB is a glycoprotein expressed on primed T CD4+ and CD8+ T cells) (Example 8). The specification also discloses primary and E1B deleted Adenovirus-infected liver cells armed with anti-gp115:anti-CD28 (Example 9). The specification discloses rat NTBII tumor cells or fused tumor cells (rat NTBII and mouse SMCC-1) armed with gp115:CD28 Bi-Mab (Example 11) and use in mice, rats and humans.

The specification does not disclose that the said monoclonal antibody against a 55, 95, 115 or 210 kDa glycoprotein on HEPA 1-6 cells is readily available to the public, nor does the specification disclose a repeatable method for obtaining the said monoclonal antibody. It is apparent that the said antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. There is no disclosure in the specification of the particular epitope, nor the sequence of the protein recognized by the said antibody, and therefore a routineer would not be able to produce said antibody based on the disclosure of the specification. If the said antibody is not so obtainable or available, the enablement requirements of

35 USC 112, first paragraph, may be satisfied by a deposit of the hybridoma producing the said antibody. See 37 CFR 1.802.

There is insufficient guidance in the specification as to how to make and/or use the instant invention, including reliance on a monoclonal antibody made to a glycoprotein of 55, 95, 115 or 210 kDa on the surface of the HEPA 1-6 hepatocellular carcinoma cell line. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

6. Claims 23-84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

a. The amendatory material that is not supported by the specification and claims as originally filed is: a method of preparing a composition, and the said composition, comprising dendritic cells or macrophages that are antigen pulsed or transfected with nucleic acid encoding the said antigen and that are fused with the recited tumor cells.

b. The amendatory material that is not supported by the specification and claims as originally filed is: "or their precursors" recited in claim 43 (line 4) and claim 50 (line 10).

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 23-84 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 23, 35, 42-47, 50, 66, 68 and 77-82 are indefinite in the recitation of one or more "gp55, gp95, gp115 or gp210 antigens" of hepatocellular carcinoma cells, lymphoma cells, colon carcinoma cells or gastric cancer cells because the characteristics of the said gp55, gp95, gp115 or gp210 antigens and hence, that of the said antibodies, are not known. The use of "gp55", "gp95", "gp115" or "gp210" as the sole means of identifying the protein to which the claimed antibody is specific renders the claim indefinite because "gp55", "gp95", "gp115" or "gp210" is merely a laboratory designation which does not clearly define the claimed product, since the said designation is merely a characterization of a protein by size and may

refer to many different proteins.

b. Claims 23 and 50 are indefinite in the recitation of "cells in patient mammal" in the last two lines of the said claims because it is not clear what is meant. It is suggested that Applicant amend said claim to recite "cells of said patient mammal".

c. Claim 23 is indefinite in the recitation of "a plurality of a bispecific monoclonal antibodies" because it is not clear what is meant.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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